Ex. 15



HOW IT'S MADE HOW TO TAKE IT MISC INFO

HISTORY

Prior to ibuprofen's introduction, nonprescription pain relief was mainly provided by aspirin, marketed since 1899, and acetaminophen, introduced in 1955. Ibuprofen was developed by Boots Laboratories, a British drug manufacturer and retailer. In the early 1960s, researchers at Boots identified carboxylic acid as the agent that gave aspirin its anti-inflammatory (soothing) property.

The Boots group investigated other carboxylic acids. When they found one that was twice as strong as aspirin, they synthesized and tested more than 600 compounds created from these acids. The most active of these, propionic acid, was chosen for clinical trial. It proved to be ineffective in treating rheumatoid arthritis. The



researchers next turned to other compounds they had synthesized from phenylalkanoic acids, which seemed to offer broader anti-inflammatory features. The most effective and useful of these was ibuprofen, which Boots began to sell in 1964 in the United Kingdom as the prescription medication Brufen.

IBUPROFEN COMES TO USA

In 1974, ibuprofen first appeared in American pharmacies after Boots granted a nonexclusive license to the Upjohn Company, which marketed ibuprofen as the prescription arthritis-relief drug Motrin. A few years later, Boots began selling its own prescription-form ibuprofen, called Rufen, in the United States.

When the United States Food and Drug Administration approved OTC sales of ibuprofen at a lower dose than in prescription form, two major drug companies immediately geared up for major production. The Whitehall Laboratories division of American Home Products came out with Advil. This was soon followed by Nuprin, which was produced by Upjohn and marketed by Bristol-Meyers.

Both companies operated under licenses from Boots, which held the worldwide patent for ibuprofen until May 1985. The companies also held exclusive marketing rights until September 1986. After that date, new manufacturers jumped into the lucrative market with products of their own, including Johnson & Johnson with Medipren, Thompson with Ibuprin, and a number of other companies with generic and private-label brands.

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